Reproductive Health Ph.D. Program

Program coordinator: László Kovács, M.D., Ph.D., D.Sc.

Ph.D. Thesis

CHARACTERIZATION OF TWIN AND MULTIPLE PREGNANCIES IN A TERTIARY CENTER IN HUNGARY

Ildikó Nyirati, M.D.

Tutor: György Bártfai, M.D., Ph.D., D.Sc.

University of Szeged

Department of Obstetrics and Gynecology

Director: Attila Pál M.D., Ph.D.

2001

Reproductive Health Ph.D. Program
Program coordinator: László Kovács, M.D., Ph.D., D.Sc.

PH.D. THESIS

CHARACTERIZATION OF TWIN AND MULTIPLE PREGNANCIES IN A TERTIARY CENTER IN HUNGARY

Ildikó Nyirati, M.D.
Tutor: György Bártfai, M.D., Ph.D., D.Sc.

University of Szeged
Department of Obstetrics and Gynecology
Director: Attila Pál M.D., Ph.D.

2001

Introduction

Twinning rates vary greatly in different parts of the world, mostly because of variations in DZ twinning. The incidence of MZ twins appears to be relatively and remarkably constant all over the world: between 3 and 4 per 1000 deliveries. Since the early 1970s, however, the incidence of twin and multiple gestations has increased dramatically, due to the growing use of ovulation induction drugs, mainly FSH stimulation and other operative-assisted reproductive techniques.

Newborn twins tend to be smaller than singletons. A fetus of a twin pregnancy usually manages to grow at the same rate as a singleton for the first two trimesters. From gestational week 30-32 onward, the rate of growth decreases relative to that of singletons. MZ twins are lighter than DZ twins and their intrapair birth-weight difference is greater. In MZ twins a birth-weight discrepancy is described as being mainly due to the feto-fetal transfusion syndrome and the excentric insertion of one of the umbilical cords. Recent studies suggested that a growth discordance may be noted earlier than previously observed. It was found that the smaller sibling displayed a lower rate of growth as early as weeks 23-24 of gestation. The birth-weight of twins appears to be unrelated to birth order. Most recent studies have found no significant differences in weight between the first- and second-born.

The greater the number of fetuses, the earlier labor is likely to start. The average length of gestation for twin pregnancies is approximately 260 days, i.e. 3 weeks shorter than the 280 days for singletons. Mean birth-weights vary to an extraordinary degree between populations. Pregnancy at high altitude substantially slows intrauterine growth and great variations can therefore be found within a given ethnic group. A strong relationship between mean birth-weight and socioeconomic status within a community was found in data collected from a number of comparative studies. Cigarette smoking by a pregnant woman reduces the growth of the fetus and increases the rate of prematurity. A positive association has been reported between the fetal growth rate and the maternal age and parity. A clearly positive correlation was established between the maternal stature, and especially the maternal height and the neonatal birth-weight. Mothers of growth retarded-newborns often exhibit chronic ill-health, involving mainly respiratory- or heart- diseases, hypertension and pyelonephritis. On the other hand, maternal diabetes enhances the rate of growth of the fetus. Pregnancy-induced hypertension (PIH) and preeclamptic toxemia also seem to have negative effects on fetal growth. Intrauterine growth retardation (IUGR) due to uterine factors is thought to be related to

insufficient uteroplacental perfusion. Infections also have been suggested as possible etiologies of IUGR. Major congenital malformations in general are also associated with slow intrauterine growth. IUGR is mostly defined as a birth-weight < the 10^{th} percentile of the gender-specific birth-weight standard for the given gestational age, but it is defined more recently as reflected by the birth of an infant weighing less than the genetic growth potential.

Despite improvements of both obstetric and neonatal care, the risks to twin fetuses and newborns remain at least 3 times those for singletons. The main factors responsible for the increased perinatal morbidity and mortality rates of twins are prematurity, IUGR of one or both fetuses, and their complications. According to the accepted definition of preterm birth (less than 37 weeks of gestation), 8.5% of singletons and 50% of twins are born preterm. In recent decades the incidence of perinatal mortality has decreased due to the improvements in obstetrical management; nevertheless, no significant changes in stillbirth rate in multiple pregnancies were found in a 22-year period. Intrauterine fetal death (IUFD) of one twin in the second or third trimester could be complicated by serious adverse effects on the mother and the surviving fetuses. Reported monofetal intrauterine death occurs in 0.5-7.0% of all multiple pregnancies, and the most appropriate explanations of death are placental insufficiency, cord entanglement, IUGR, discordant growth, twin-to-twin transfusion syndrome, and fetal malformation.

CTG is a noninvasive diagnostic method that is used most frequently for the intrapartum monitoring of fetal well-being. It records fetal heart rate, fetal movements and uterine activity simultaneously. The great advantage of CTG is that it can be repeated unrestrictedly, allows an immediate assessment and provides continuous registration in contrast with periodic auscultation. It is important to point out that the evaluation of cardiotocograms depends on the stage of labor. In clinical practice, we can distinct three stages as concerns the instrumental monitoring of labor: 1. the start of pains (the latent phase of the first stage of labor), 2. the active phase of the first stage of labor, 3. the second stage of labor. Intrapatum monitoring gives information on the placental reserve capacity. In cases of signs indicating fetal hypoxia, safe labor management can be established only by close and conscientious monitoring, including the application of fetal pH control. On the basis of the fetal movements, four sleep-awake states can be distinguished, according to which Nijhuis identified four specific CTG traces. A permanent decrease in placental reserve capacity triggers signs of hypoxia that can be observed in the CTG trace.

Twinning is a unique challenge for both the medical staff and the parents during pregnancy, delivery and the child-bearing age. In the early postpartum period the mothers of twins have to contend with the difficulties and disappointments of breast-feeding. Differences in the compositions of human milk and unmodified cow's milk have been known for many years. Recent studies of the nutritional needs of infants and advances in technology have led to the development of more adequate infant formulas, but all experts agree that human milk is the best infant nutrition.

AIMS OF THE STUDY

1. Characterization of multiple pregnancies, deliveries and newborns in a tertiary center in Hungary.
2. Study of the occurrence of intrauterine fetal death in multiple pregnancies.
3. a) To examine the sleep-awake periods for singleton and twin fetuses during the last three hours of the second stage of labor (active phase), using continuous CTG traces.
   b) To compare the number of fetal sleep-awake periods, F4 periods and decelerations with the neonatal outcome.
4. Study of the effects of early and simultaneous breast-feeding of twin newborns.

MATERIALS AND METHODS

At the Department of Obstetrics and Gynecology of the University of Szeged, a retrospective analysis was made of all multiple births of more than 24 weeks of gestation between 1 January, 1991 and 31 December, 1999. During this 9-year period, the total number of deliveries was 18173, of which 431 were multiple gestations, i.e. an the incidence of 2.37%. 402 twin, 26 triplet and 3 quadruplet pregnancies were recorded. Gestational age was calculated on the basis of the first day of the LMP and was confirmed by the results of early US examination. If the difference was more than 7 days, the US result was considered valid.

Birth-weight discordance was defined as the percentage difference between the multiple siblings, calculated as [A-B]/A*100 (A = birth-weight of the largest twin, B = birth-weight of the smallest twin).

CHARACTERIZATION OF TWIN PREGNANCIES, DELIVERIES AND NEWBORNS IN A TERTIARY CENTER IN HUNGARY

The mean maternal age and primiparity were similar in the twin and triplet pregnancies. There was no difference in pre-pregnant maternal body mass index (BMI), but the mean maternal weight gain was higher in triplet gestations. The frequency of preeclampsia was very high in both groups. Gestational diabetes was found in 19.2% of the triplet pregnancies, in contrast with 3.5% in the twin pregnancies. Due to cervical incompetence, operation with cervical cerclage was needed in 14.9% of the twin and 73.6% of the triplet pregnancies. Intravenous tocolysis was administered in 36.1% of the twins and 42.3% of the triplets. Among the twin gestations 20.9% resulted from assisted reproduction, as compared with 73.0% among the triplets. Most of the twin babies was delivered in the 34th weeks of gestation, and 60.7% of the twins were delivered before 37 completed weeks. Preterm delivery (< 37 weeks) was registered in 84.2% of triplet pregnancies. The mean gestational age was 247.7 days (35.4 weeks) in the twin pregnancies and 236.4 days (33.9 weeks) in the triplet pregnancies. The mean birth-weight of the triplet newborns was considerably lower than that of the twin babies, and the mean birth-weight of the consecutive newborns was much lower. The mean birth-weight of the first twin was 2226.2 g and that of the second twin 2209.9 g. The birth-weight of the boys was higher than of the girls (2263.4 vs 2173.7g), but the difference was not significant. In 62.7% of the twin newborns the birth-weight was below 2500 g; in 5.7% of the cases the neonatal birth-weight did not reach 1000 g. Most of the twin pregnancies demonstrated a low birth-weight for both neonates. Both newborns were delivered with a normal birth-weight in only 26.2% of the cases, and in 4.0% both babies had a very low birth-weight. Discordant growth, when the difference between the largest and the smallest newborn was more than 15%, was found in 27.6% of the twins and 60.8% of the triplets. The difference exceeded 25% in 8.9% of the twins and 42.3% of the triplets. In 63.6% of the twin pregnancies, vaginal (or operative vaginal) delivery was available. The pregnancy was terminated by Cesarean section in 36.5% of the twins and in 89.5% of the triplets. Unfortunately there was a very high rate of missing data as concerns placentation (25.1%). We found bichorionic-biamniotic placentation in 53.7% of the twin gestations and monochorionic-monoamniotic placentation in 2.3% of the cases. The frequency of an Apgar score < 7 at 5 min was similar for the first and second twins and it was twice as high as for the first and second triplet newborns and three times as high as for the third triplets. The umbilical cord blood pH was not measured in all newborns, but the pH level of the

consecutive newborns was much higher. In consequence of prematurity or immaturity, more than one-fifth of the twin newborns and 42.3% of the triplet newborns were transferred to the NICU. Intrauterine death occurred in 1.6% of the twins and 5.1% of the triplets. Early neonatal death (within 168 h) was very high for both twin and triplet newborns.

There were significant differences between spontaneous versus induced multiples in the rates of maternal complications during pregnancy. Gestational diabetes and incompetent cervix requiring treatment by cerclage were more frequent in the induced twin group than in the spontaneous one. Interestingly, the rate of preeclampsia was significantly lower in the induced triplet pregnancies (17.6%) as compared with the spontaneous triplets (33.3%). The numbers of patients with threatened preterm delivery were similar among the induced and the spontaneous twins and triplets. The gestational ages at delivery were similar in the spontaneous and induced groups. Operative vaginal delivery and Cesarean section were more common in the induced than in the spontaneous twin group. Cesarean delivery was performed in all the spontaneous triplet pregnancies, in contrast with the induced group, where rapid vaginal delivery occurred in 2 cases. There was no statistical difference between the induced and spontaneous twins as concerns the mean neonatal birth-weights of twin A and twin B. Among the induced triplets, the birth-weights of the first and second newborns were significantly lower than those of their spontaneous counterparts. The Apgar score and the umbilical cord blood pH were much worse in both induced groups. Transfer to the NICU was significantly more common in the induced newborns. We defined growth discordance as a birth-weight difference of at least 25%. On this basis, 14.7% of the induced twin newborn pairs showed discordant growth, in contrast with 7.3% of the spontaneous twins. The difference between the triplet groups was not significant in respect of a birth-weight discordance. The perinatal mortality rates were similar in the twin groups, but the rates of IUFD and early neonatal death (within 168 h) differed significantly. In the triplets, early neonatal death was extremely high (19.6%) in the induced group, and intrauterine death also occurred more frequently than in the spontaneous triplet group.

Study of survival probabilities of twin fetuses: Intrauterine fetal death in twin pregnancies

In the multiple pregnancies the intrauterine fetal death of 1 fetus occurred in 13 cases (3.1%) and both fetuses died in another 2 cases (0.5%). Nine gestations were conceived spontaneously, and 6 resulted from assisted reproductive techniques. All but 2 pregnancies in

the studied group were complicated by threatened preterm delivery and 3 of the 15 were terminated at term. In 2 triplets and 1 twin pregnancies, cervical cerclage according to McDonald was performed due to cervical incompetence. Pregnancy-induced hypertension, gestational diabetes mellitus and severe preeclamptic toxemia with an episode of antepartum eclampsia were noted. The fetal surveillance assessment was achieved by CTG and blood flow velocity waveform analysis. Both methods were applied in 8 pregnancies, and only the non-stress test in 1 pregnancy. With the exception of 3 triplet pregnancies, non-reassuring tests of CTG or/and flowmetry of the umbilical artery were performed before the diagnosis of intrapartum fetal death. In 6 cases, neither CTG nor flowmetry was carried out and fetal death occurred before admission to our Department. The gestational age ranged between 24 and 38 weeks. Three mothers with triplets underwent Cesarean section and 2 twin pregnancies were terminated by Cesarean section due to the breech presentation of the first fetuses, and in 1 induced twin pregnancy Cesarean section was performed because of the onset of labor at 25 weeks of gestation and the pregnancy was complicated by severe toxemia and eclampsia. The estimated time that elapsed between fetal death and delivery varied from a few hours to 14 days; in 2 cases the time was not identifiable. Discordant growth was registered in 9 cases out of 15. Intrauterine fetal death in the twin pregnancies occurred more often in monochorionic (60%) than in bichorionic (40%) placentation. In the triplet pregnancies, 2 placentas were trichorionic, 1 was bichorionic-triamniotic and the fourth one was monochorionic-triamniotic. The causes of intrauterine death were established by autopsy. Placental insufficiency/infarction of the placenta was registered in 7, infection in 2, severe IUGR and placental abruption in 1 case. Two stillborn neonates had omphalocele with congenital cardiac malformations with various minor abnormalities. Both fetuses in the monochorionic-monoamniotic twin gestations died intrauterine. The fetuses in one of the monoamniotic pregnancies displayed manifest signs of the twin-to-twin transfusion syndrome. No obvious cause of intrauterine death could be found in the other monoamniotic pregnancy and in one of the triplet pregnancies. The pregnancy was prolonged in 5 cases, without any coagulation disorders in the maternal coagulation profile. Two live-born neonates died within a few hours because of extreme immaturity, with birth-weights of 580 and 550 g. Late neonatal death was registered in 1 immature newborn weighing 1100 g at delivery, and another 7 infants were treated in the NICU; they were discharged after 10-25 days. One of the surviving twins had minor congenital anomalies. In our registry, there was no trace of any early sequel of IUFD.

EXAMINATION OF INTRAPARTUM CARDIOTOCOGRAMS AND SLEEP-AWAKE PERIODS IN SINGLETON AND TWIN FETUSES DURING THE SECOND STAGE OF LABOR

The intrapartum cardiotocograms of 300 singleton and 42 twin pregnancies between weeks 28 and 42 of gestation were subjected to retrospective analysis. The recordings were made with Kranzbühler, Hewlett Packard and Oxford Sonicaid Team cardiotocographs. The advantage of the latter two cardiotocographs is that they have the ability to record twin fetuses simultaneously. The continuous intrapartum cardiotocograms of the last 3 h of the first stage of labor in vaginal deliveries, and of the last 3 h before resorting to Cesarean section, were selected into the study. Good trace-quality and low sign-loss were important criteria. In addition to the above-mentioned criteria, in twin pregnancies, only traces simultaneously recorded with the same cardiotocograph were accepted. Visual analysis was made separately by two CTG experts to eliminate intra-observer variance in the interpretation of traces. Fetal movements were evaluated in accordance with the "Fetal Movement Profile" (FMP) criteria (F1-F4). Decelerations were defined as periods with an amplitude > 20 beats per min below the baseline and duration > 30 s. In 62% of the traces, FMP was assessed cardiotocographically, and the number of fetal movements was given by the device as a percentage every tenth minute. This was of great help in the analysis especially as concerns differentiation of the F2 and F4 periods.

Data concerning the pregnancies and the condition of the neonates were obtained from the case histories. The venous umbilical cord blood pH was registered in the database. The pH measurements were performed with a Gem Premier Plus device. The neonate was not considered healthy if signs of growth retardation were present, the venous cord blood pH was less than 7.20, the 5-min Apgar score was less than 7, the neonate was referred to the NICU and the reason for the referral was not a low birth weight. The average age of the mothers in the singleton pregnancies was 26.7 ± 4.5 years, while in the twin pregnancies it was 29.8 ± 4.1 years. The proportion of premature rupture of membranes was high in both groups (33.7% in the singleton pregnancies and 40.5% in the twin pregnancies). The administration of oxytocin infusion during labor was necessary in 68.7% and 66.7% in the two groups. In our study, the average gestational age was 39 weeks in the singleton and 35 weeks in the twin pregnancies. The proportion of premature births was 10 times higher in the twin pregnancies than in the singletons. The rates of spontaneous vaginal delivery were 71.7% and 65.7% in the two groups. A majority of the neonates were born in good general condition, with a normal cord blood pH and Apgar score. In 1.3% of the singletons and in 9.5% each of twins A and B, we found low 5-

min Apgar scores (<7). The venous cord blood pH was lower than 7.20 in 22% of the singleton neonates, in 7.1% of the A siblings and in 14.2% of the B siblings. 1.7% of the singletons, 11.9% of twins A and 19% of twins B were referred to the NICU for reasons other than low birth-weight. In the final evaluation of the intrapartum CTG traces, we did not find a significant ($p<0.05$) difference between the fetal heart rates of twins A and B or between those of the twins and the singletons. The average of the changes in the sleep-awake periods was between 4.3 and 4.8. In the last 3 h of the first stage of labor, the fetuses exhibited the characteristic picture of the awake period (F4) 2.1-2.5 times on average. We found an F3 period in only 7 traces (2.3%). The average number of decelerations in the above-mentioned 3 h section of the CTG traces was between 4.7 and 4.9. On the basis of the venous cord blood pH values, three subgroups were created: 1) <7.20, 2) 7.20 - 7.25 and 3) >7.25. Significant differences were found ($p<0.05$) as concerns the number of periodic changes, and the occurrence of F4 periods and decelerations in the different pH subgroups in the singleton pregnancies. Similar differences could be observed for the twin A and B fetuses, but, because of the low number of cases, significance could not be calculated.

In the second part of the study, we created subgroups on the basis of the occurrence of sleep-awake period changes and F4 periods and examined the condition of the neonate (based on the venous pH) according to the occurrence of these factors. More period changes and more F4 periods were related to a better neonatal condition (higher venous pH values) both in the singletons and in the twins. This phenomenon revealed a statistically significant deviation when the subgroups of singleton pregnancies were compared ($p<0.05$). In the twin pregnancies, however, we could not perform a statistical test because of the low number of cases.

Study of the effects of early and simultaneous breast-feeding of twin newborns.

A retrospective analysis was made of all twin pregnancies with at least 24 weeks of gestation at our Department between 1 January, 1994 and 31 December, 1998. During this period, 232 were multiple pregnancies (215 twins, 15 triplets and 2 quadruplets). The pregnancies with IUFD or major congenital malformations were excluded as were the pregnancies in which the birth-weight of each newborn was less than 2000 g. On the basis of the birth-weight, three groups were created: (1) each newborn had a birth-weight of 2000-2500 g, (2) the largest newborn had a birth-weight of at least 2500 g and (3) each newborns had a birth-weight of at least 2500 g. Early breast-feeding was considered as breast-feeding of the newborn

immediately after vaginal delivery or 1.5-2 hours after Cesarean section with epidural analgesia or 6 hours after in cases with general anaesthesia. Of the 15 triplet pregnancies, two met the criteria of the group 1 and 4 met the criteria of the group 2. The mean maternal age, primiparity and pre-pregnant maternal BMI did not yield significant differences. In the pregnancies where each newborn had a birth-weight of > 2500 g, the mean maternal weight gain was significantly higher than in the other groups. Since the groups were created on the basis of the newborns' birth-weight, the mean birth-weights were automatically significantly different in each group. As expected, the mean gestational ages were also different in the groups. Two-thirds of the newborns in group 1 were transferred from our Department during the first 2 days, while 8.3% of the twins in group 3 were a transferred to the NICU. Early breast-feeding could be carried out in only 10 pregnancies (29.4%) in group 1, 89.1% in group 2 and 95.0% in group 3. In the cases involving early breast-feeding, all of the mothers required rooming-in accommodation. There were no significant differences according to the duration of neonatal jaundice and the duration of stay at our Department. More than 80% of the newborns with early breast-feeding in each group were exclusively breast-fed at discharge. In the 3 triplet pregnancies, where the newborns were early breast-fed, each baby suckled well and the mothers had enough milk for their 3 newborns at discharge.

Discussion:

Characterization of multiple pregnancies, deliveries and newborns in a tertiary center in Hungary.

The perinatal morbidity and mortality rates in multiple gestations are 4 to 10 times higher than in singletons. The high perinatal morbidity and mortality in multiples are associated with increased rates of prematurity, low birth-weight and IUGR. Because of the higher perinatal morbidity and mortality rates, mothers with multiple gestations should be provided with extra ante-, intra- and postnatal care. Our study confirms that maternal complications and an unfavorable perinatal outcome are more common in induced than in spontaneous multiple pregnancies. Numerous investigators have noted an increased incidence of preeclampsia among multiples compared with singletons. We observed a high incidence in all groups, but surprisingly a significantly lower incidence of preeclampsia was found in the induced triplet pregnancies than in the spontaneous group. The rate of premature deliveries was similar in spontaneous and induced pregnancies. We found an increased rate of Cesarean delivery in

induced as compared with spontaneous multiple gestations. Discordant growth among multiple fetuses suggests a heightened degree of risk, with a medical and economic consequences of high-level care in a special center for these fetuses and newborns. In our study, the number of pregnancies with discordant birth-weights was very high, especially in the induced twin group. One-third of the induced triplet pregnancies were complicated by discordant growth.

Study of the occurrence of intrauterine fetal death in multiple pregnancies.

In twin pregnancies, IUFD is 2-4 times more frequent than in singleton pregnancies. This risk is even greater in triplet pregnancies. A close association has been reported between PIH or preeclampsia and fetal death. In our study, 2 of the 13 women (15.4%) suffered from hypertension disease. Placental factors such as placental insufficiency and anemic infarction of the placenta were the most probable causes of fetal death. There were 2 monoamniotic gestations and both of them were complicated by the death of both fetuses. In one of these monoamniotic gestations one fetus was anemic, while the other was polycytemic, and a severe discordance was found due to twin-to-twin transfusion. In our study, a severe discordance was diagnosed in 54% of the cases. The risk of maternal coagulopathy after intrauterine fetal death in singleton pregnancies was reported. However, disseminated intravascular coagulation the mother after monofetal death in multiple pregnancy is a very rare event. There was no maternal coagulopathy in our studied group.

On the basis of our clinical survey, the recommended clinical policy is as follows: In gestations of more than 36 weeks complicated by IUFD, induced delivery is recommended. Between 24 and 36 weeks, termination of pregnancy is advised if fetal or maternal complications occur.

Examinations of the sleep-awake periods for singleton and twin fetuses during the last three hours of the second stage of labor (active phase), using continuous CTG traces.

Intrapartum monitoring has a significant role in the early recognition of fetal compromise. Labor involves a significant stress for the fetus. Intrapartum monitoring helps the obstetrician to distinguish physiological stress from distress. Fetal distress is a sign of the inability to cope with intrapartum stress, a condition which may lead to asphyxia. The latter is characterized by hypoxia and acidosis. Frequently, we can determine certain factors which endanger fetal well-being as early as the antepartum period. In such cases, intrapartum

monitoring helps prevent the development of hypoxic complications. In our study, we chose the active phase of the first stage of labor to examine the fetal sleep-awake periods and the changes in fetal heart rate that emerge in response to intrapartum stress. The mature and healthy fetus spends 60-70% of its time in the F2 state in the antepartum period (length: 34±6 min) and 25% in the F1 state (length: 17±8 min). In 6% of the time, no fetal movement can be observed and the variability of the baseline is low (7±0.5 bpm). Our study has showed that sleep-awake periods can be observed in healthy fetuses in the intrapartum period too, that awake (F4) states supervened 2 times in the examined 3 h-long period, and that changes in sleep-awake states occurred 4 times. Therefore, we can state that fetuses spend most of their time in the F1 and F2 states in the intrapartum period, similarly as found in antepartum surveys.

Comparison of the number of fetal sleep-awake periods, F4 periods and decelerations with the neonatal outcome.

Higher venous cord blood pH values accompany a greater number of period changes and a greater number of F4 states, while a higher occurrence of decelerations is associated with a lower venous cord blood pH. In 1 singular pregnancy, the fetus remained in the F1 state throughout the 3 h period, and it was born with a venous cord blood pH of 6.96 and with 1, 5 and 10-min Apgar scores of 3, 6 and 10. Thus, we can conclude that the exclusive presence of a sleep state and few sleep-awake period changes may be ominous signs of fetal hypoxia.

One of the current great challenges for obstetricians is that more and more mothers want 'natural labor' and a thoroughly healthy baby. Although labor is a physiological process, it is well known that 'normal labor' is a retrospective diagnosis. Intrapartum CTG monitoring helps us to recognize not just severe fetal hypoxia: through analysis of fetal sleep-awake periods, it also enables us to realize the risk of intrapartum stress converting into distress. In this way, we can take measures in time to prevent the development of asphyxia. The continuous recording of fetal movements together with the fetal heart rate would also provide a significant help to the obstetrician in the first stage of labor.

Study of the effects of early and simultaneous breast-feeding of twin newborns.

Until the 20th century, human milk was the only source of nutrients for infants after birth. From the beginning of last century, with the decline of breast-feeding, evaporated milk and infant formulas were gradually applied. After World War II, modified evaporated infant

formulas were replaced universally. In the USA, a large nationally representative sample of mothers who were surveyed by mail-questionnaires was analyzed to determine the trend of breast-feeding in hospital and up to 6 months of age at home. The data indicated that approximately 14% of infants 2 months of age were breast-fed in 1971. From that year on, they noticed an increasing trend in both the incidence and duration of breast-feeding. This occurred at all ages and in all demographic categories surveyed. Two main factors influence the initiation of breast-feeding: maternal and family attitudes towards breast-feeding; and the attitudes of the health-care staff who come into contact with the mothers and neonates prenatally, intrapartum and postnatally. Most women know that mother's milk is the best for newborns. The new parents need personal advice from the obstetrician and the health counselor, who discuss with them the option of breast-feeding. The first few weeks of lactation usually have a critical role as regards the outcome and duration of nursing. The first feeding should be accomplished as soon as possible and whenever the infant is hungry after that. The important factors are the time of nursing, the frequency of feedings, the availability for demand feeding, the positioning during breast-feeding and the total time spent suckling a day. The more frequent the suckling, the quicker the milk production. Any kind of supplementation of a breast-fed newborn is reported to delay the arrival of true milk. Most primiparous mothers require encouragement to promote milk production. The medical staff involved in the care of the new mother should therefore be well informed about the physiologic principles of lactation, the preparation of the breast, and the management of breast-feeding. In recent papers, the importance of early and repeated contacts with a health-counselor has been described, which is associated with a significant increase in breast-feeding exclusivity and duration. Exclusive breast-feeding was practised by 67% of mothers who were visited 6 times, and by 50% of mothers who were visited 3 times by a health-counselor, as compared with only 12% of control mothers at 3 months postpartum.

All mothers at our Department are seen by a lactation consultant. She helps mothers in the initiation of breast-feeding after delivery and follows up frequently until their discharge from the Department. If the newborns are able to nurse, each baby's suckling effectiveness is evaluated by measurement of the infant's weight. Our data confirmed that breast-feeding mothers and their newborns spend a shorter period in the maternity ward. It was reported that mothers of twins were less likely either to initiate breast-feeding in the hospital or to continue nursing at 6 months postpartum as compared with all mothers. Twins can be nursed successfully, but the breasts have to be regularly and effectively emptied. The first postpartum

week is an extremely critical period in the establishment of lactation. During this period, inadequate emptying of the breasts is probably the main leading cause of a milk insufficiency. Whenever any doubt exists about either twin's ability to empty the breasts regularly, the mother is advised to use an electric breast pump in order to empty her breasts fully after each nursing.

Numerous positions for the simultaneous nursing of twins have been described. The practice in our hospital is to advise mothers concerning simultaneous breast-feeding, and the lactation consultant helps them find the most convenient position. The simultaneous nursing of twins has the important advantage of being time-efficient and of allowing the more vigorous baby to stimulate the milk-ejection reflex for both of them. It is still controversial whether same-breast nursing minimizes cross-contamination, but allowing the more vigorous infant regularly to suckle both breasts helps to stimulate adequate milk production bilaterally. Simultaneous nursing may generate a higher maternal prolactin response during breast-feeding, which may help to stimulate increased milk production. The main drawback of simultaneous nursing is that it does not permit the mother to give each baby her individual and undivided attention during feedings.

After Cesarean section some modifications of the early breast-feeding routines are necessary. Whenever the mother's condition permits, attempts should be made for the newborn to perform the first suckling. As about 50% of twin pregnancies result in premature delivery, the mothers need to be instructed on appropriate techniques of production, collection, maintenance and storage of her milk as soon as possible following delivery, even though her infant may not be feeding for several days or weeks. One of the major stresses for parents of twins is infant feeding in the early postpartum period. Breast-feeding is often a disappointing experience because of the almost continual feeding in the first days and the fear of insufficient milk production. The use of an electric breast pump to provide the required milk yield, practical advice about breast-feeding techniques and nursing positions, and the lactation consultant's follow-up during the hospital stay should facilitate successful breast-feeding among mothers of twins.

Our study confirmed that, under optimal circumstances, the breast is capable of producing sufficient milk to nourish two, and even three infants. As milk production is a very important factor in the successful nursing of twins, in the early postpartum period every effort should be made to maximize the milk supply. Once lactation is well established, most of the mothers of twins find breast-feeding more convenient than bottle-feeding.

ACKNOWLEDGEMENTS

I wish to express my grateful thanks to my Ph.D. tutor, Professor György Bártfai M.D., Ph.D., D.Sc., for his professional guidance.

I am deeply indebted to Professor László Kovács M.D., Ph.D., D.Sc., Director of the Reproductive Health Ph.D. Program, for his helpful discussions.

I am grateful to Professor Attila Pál M.D., Ph.D., Director of the Department of Obstetrics and Gynecology, University of Szeged, for all his kind help.

My thanks are due to the midwives of the CTG laboratory for their great help.

I am especially grateful to my family for their patience and support.

PUBLICATIONS RELATED TO THE SUBJECT OF THE THESIS

1. Nyirati I., Orvos H, Bártfai Gy, Kovács L: Iatrogenic multiple pregnancy: Higher risk than a spontaneous one? J Reprod Med 1997 (42) 695-698
2. Nyirati I, Foroughi E, Hodoniczki L, Bártfai Gy, Kovács L: Számítógéppel vezérelt kardiotokográfia és az arteria umbilicalis véráramlás mérésének egyidejű alkalmazásával szerzett tapasztalataink. Magyar Nőorvosok Lapja 1997 (60) 174-176
3. Tarnai L, Nyirati I, Bánfalvi A, Bártfai Gy, Herczeg J: Antepartum magzati szívhangészlelés során előforduló hibalehetőségek. Magyar Alapellátási Archivum 1999 (4) 254-256
4. Blickstein I, Goldman RD, Kupferminc M, etc., Nyirati I, Bártfai Gy, etc.: Delivery of breech first twins: A multicenter retrospective study. Obstet Gynecol 2000 (95) 37-42